

REMARKS**The Amendments**

Claim 1 is amended for clarification purposes and to incorporate the substance of claim 2 into claim 1. Claim 17 is amended so that it is rewritten in independent form. The new claims are fully supported by the disclosure, see, e.g., the original claims. An obvious correction to claims 7-9 is also made.

To the extent that the amendments avoid the prior art or for other reasons related to patentability, competitors are warned that the amendments are not intended to and do not limit the scope of equivalents which may be asserted on subject matter outside the literal scope of any patented claims but not anticipated or rendered obvious by the prior art or otherwise unpatentable to applicants. Particularly, the upper limit of 90% of the amount of dangling crosslinkers in the claims should not be considered to preclude equivalents coverage of higher amounts since higher amounts are even further removed from any prior art teachings. The 90% recitation was included due to the restrictions of written description support in the original disclosure. It was not foreseen for the original disclosure that the amount range reciting a maximum between 90 and 100% would be necessary. But dangling crosslinker amounts higher than the 90% would be essentially practicing applicants' invention. Applicants reserve the right to file one or more continuing and/or divisional applications directed to any subject matter disclosed in the application which has been canceled by any of the above amendments.

The Rejection Under 35 U.S.C. § 112, Second Paragraph

The rejection of claims 1-18 under 35 U.S.C. § 112, second paragraph, is respectfully traversed.

Claim 1 is amended for clarification purposes to recite a “hydrogel polymer prepared using an excess amount of cross-linker” and to recite that the “amount of dangling cross-linkers, based on the total amount of cross-linkers bound to the polymer by at least one functional group, is from 20% to 90%.” It is believed that these clarifications render both grounds of the rejection moot. Thus, the claim now recites that the hydrogel is prepared by treatment with excess cross-linker rather than a hydrogel is prepared and then subsequently treated with crosslinker. Further, the particular extent of dangling cross-linkers is recited which also quantifies the extent of cross-linkers bonded at two functional groups since they would be the remainder of cross-linkers that are not dangles.

Accordingly, the rejection should be withdrawn.

The Rejections Under 35 U.S.C. § 102

The rejections of claims 1-16 and 18 under 35 U.S.C. § 102, as being anticipated by Mooney (WO 98/12228) and Bouhadir (Polymer, 1999) are respectfully traversed. These two references stem from the same research and contain, in relevant part, essentially the same disclosure; thus, they will be discussed together.

Both references teach hydrogels prepared by crosslinking a poly(aldehyde guluronate) derivative of alginate with adipic acid and other manners of crosslinking; see, e.g., Mooney, page 15, line 27, to page 24, line 5, and Examples 10-19. Both teach that full or maximized crosslinking with the crosslinking agents is desired, as opposed to partial crosslinking (i.e., dangles); see, e.g., Mooney, page 56, lines 5-17, and Bouhadir, paragraph bridging pages 3575-3576, first full paragraph on page 3580.

Both references recognize the possibility of dangling crosslinkers, i.e., crosslinkers bonded at only one of their two functional groups, but neither discloses that such dangling crosslinkers are desired and both speak in terms of maximizing the amount of full

crosslinking. This is contrary to the instant invention wherein it has been found that a purposefully provided significant extent of dangling crosslinkers gives desirable properties for the purposes of the invention.

Certainly, neither references discloses a hydrogel polymer which contains as much as 20% of the attached crosslinking groups being dangling crosslinkers, let alone as much as 30%. Compare the instant claims.

While Mooney is silent as to any particular degree of dangling crosslinkers, Bouhadir specifically addresses the extent. Bouhadir states that the “efficiency of the crosslinking reaction ranged between 84 and 96% at all reaction conditions.” This efficiency is a measure of the amount of complete crosslinks as compared to dangling crosslinks and, thus, reflects an amount of dangling crosslinkers of from 4 to 16%, i.e., below 20%. Contrary to the allegation in the Office Action, the determination of crosslinking efficiency discussed in Bouhadir and in the present specification is not different. They are the same but expressed in Bouhadir as the complementary value of amount fully crosslinked per amount of crosslinker reacted. See the discussion of the method of determination by the TNBS assay at part 2.3 of Bouhadir compared to page 11, first full paragraph, describing the same assay. Applicants disagree that Figure 4 shows > 20% dangling crosslinkers compared with the total amount of bound crosslinker. Figure 4 shows about 250 μmol fully crosslinked and about 50 μmol partially crosslinked. This corresponds to one sixth, or 16%, dangling crosslinkers which complements the 84% crosslinking efficiency taught by Bouhadir. Furthermore, Figure 4 certainly does not support disclosure of as high as 30% dangling crosslinkers.

As to Mooney's Example 19, the Office Action appears to allege that the example is conducted in a same or similar manner to the examples of the instant specification and, therefore, would inherently provide the same amount of dangling crosslinkers. This allegation is not supported, however. The 6% w/w of PAG used in Mooney's Example 19

means that a very diluted amount of polymer was provided, thus, affording less opportunity for crosslinking with the adipic acid. This is confirmed by the fact that at 4% w/w of PAG in Example 19, no crosslinking reaction of any significance occurred and the extent of crosslinking increased as the concentration of PAG was increased. Further, the first full paragraph on page 56 of Mooney describes that, with a 6% w/w of PAG, increasing the concentration of adipic acid maximized the mechanical strength at 150 mM which is an indication of maximal full crosslinking, i.e., approaching 100% full crosslinking or 0% dangling crosslinkers. Increasing the concentration of adipic acid from that point decreased the extent of full crosslinking (see Figure 14) but no inference is made that the amount of dangling crosslinkers would amount to as high as 20%, certainly not 30%. In fact, Example 19 is best compared to the example shown in Figure 4 of Bouhadir discussed above wherein a maximum of 16% dangling crosslinkers was achieved. Finally, it must be remembered that these higher amounts of dangling crosslinkers are viewed as undesirable in Bouhadir and Mooney. Thus, the references fail to motivate one of ordinary skill in the art to increase the amount of dangling crosslinkers.

To the contrary, the Example discussed beginning on page 9 of the instant specification utilizes a much more concentrated solution of PAG, i.e., 20 wt%, and would not be expected to yield the same or similar results as when utilizing a 6 wt% solution. The more concentrated solution of PAG in the specification examples means that the adipic acid solution is less diluted and able to provide the crosslinking groups for reaction with the PAG more effectively. The result is that an effective excess of available crosslinking groups is provided such that dangling groups occur in significant amount, e.g., 20% or more.

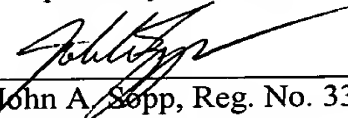
Accordingly, applicants respectfully disagree with the implication from the Office Action that Example 19 of the Mooney reference inherently results in a hydrogel polymer meeting the claimed recitations.

For all of the above reasons, it is urged that neither of Mooney or Bouhadir provide any disclosure of an embodiment meeting the elements of the instant claims. Thus, they cannot anticipate the instant claims and the rejections under 35 U.S.C. § 102 should be withdrawn. Further, the references do not support a rejection under 35 U.S.C. § 103. Contrary to suggesting modification of the reference hydrogel polymers to increase the amount of dangling crosslinkers to 20% or 30%, the references' objectives regarding crosslinkers is to maximize the extent of full crosslinking, thus, minimizing the extent of dangling crosslinkers.

It is submitted that the claims are in condition for allowance. However, the Examiner is kindly invited to contact the undersigned to discuss any unresolved matters.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



John A. Sepp, Reg. No. 33,103
Attorney for Applicants

MILLEN, WHITE, ZELANO &
BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

Attorney Docket No.: UMICH-9

Date: March 24, 2003

K:\Umich\9\Reply to 11-25-02 OA.doc

VERSION WITH MARKINGS TO SHOW CHANGES MADE**IN THE CLAIMS:**

Claims 1, 3, 4, 7, 8, 9 and 17 have been amended to read as follows:

1. (Amended) A hydrogel composition comprising a hydrogel polymer ~~reacted with~~ prepared using an excess amount of cross-linker having two or more functional groups capable of cross-linking the polymer such that the polymer has ~~a significant extent of~~ cross-links to other hydrogel polymer molecules and also has ~~a significant extent of~~ dangling cross-linkers with at least one functional group bound to a hydrogel polymer and at least one unbound functional group capable of reversibly cross-linking the polymer, wherein the amount of dangling cross-linkers, based on the total amount of cross-linkers bound to the polymer by at least one functional group, is from 20% to 90%.

3. (Amended) The hydrogel composition of claim 1, wherein the ~~cross-linking efficiency of cross-linkers with at least one functional group bound to a hydrogel polymer and at least one unbound functional group capable of reversibly cross-linking the polymer~~ amount of dangling cross-linkers is from 20% to 70%.

4. (Amended) The hydrogel composition of claim 1, wherein the ~~cross-linking efficiency of cross-linkers with at least one functional group bound to a hydrogel polymer and at least one unbound functional group capable of reversibly cross-linking the polymer~~ amount of dangling cross-linkers is from 30% to 50%.

7. (Amended) The hydrogel composition of claim 6, wherein the ~~cross-linked~~ hydrogel polymer has a weight average molecular weight of 1,000 to 50,000 dalton.

8. (Amended) The hydrogel composition of claim 6, wherein the ~~cross-linked~~ hydrogel polymer has a weight average molecular weight of 1,000 to 30,000 dalton.

9. (Amended) The hydrogel composition of claim 6, wherein the ~~cross-linked~~ hydrogel polymer has a weight average molecular weight of 1,000 to 10,000 dalton.

17. (Amended) ~~The A~~ hydrogel composition ~~of claim 1~~ comprising a hydrogel polymer prepared using an excess amount of cross-linker having two or more functional groups capable of cross-linking the polymer such that the polymer has cross-links to other hydrogel polymer molecules and also has dangling cross-linkers with at least one functional group bound to a hydrogel polymer and at least one unbound functional group capable of reversibly cross-linking the polymer, wherein the cross-linker is a compound with at least two aldehyde groups and the hydrogel polymer is a polymer containing or modified to contain hydrazide groups.

Claim 2 has been canceled without prejudice or disclaimer.

Claims 20-22 have been added.